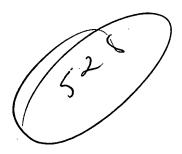
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LOGINID: ssspta1611sxp

PASSWORD:

TERMINAL (ENTER 1, 2, 3, OR ?):2



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                 PHARMAMarketLetter(PHARMAML) - new on STN
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         Aug 19
NEWS 5
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                 now available on STN
NEWS
         Aug 26
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NEWS
     7
         Sep 03
                 JAPIO has been reloaded and enhanced
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         Sep 16
                 Experimental properties added to the REGISTRY file
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         Sep 16
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         Oct 01
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         Oct 24
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         Oct 24
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         Nov 18
                 DKILIT has been renamed APOLLIT
NEWS 14
         Nov 25
                 More calculated properties added to REGISTRY
NEWS 15
         Dec 04
                 CSA files on STN
NEWS 16
         Dec 17
                 PCTFULL now covers WP/PCT Applications from 1978 to date
NEWS 17
         Dec 17
                 TOXCENTER enhanced with additional content
NEWS 18
         Dec 17
                 Adis Clinical Trials Insight now available on STN
NEWS 19
         Jan 29
                 Simultaneous left and right truncation added to COMPENDEX,
                 ENERGY, INSPEC
NEWS 20
         Feb 13
                 CANCERLIT is no longer being updated
NEWS 21
         Feb 24
                 METADEX enhancements
NEWS 22
        Feb 24
                 PCTGEN now available on STN
NEWS 23 Feb 24
                 TEMA now available on STN
NEWS 24 Feb 26 NTIS now allows simultaneous left and right truncation
NEWS 25 Feb 26 PCTFULL now contains images
NEWS 26 Mar 04
                 SDI PACKAGE for monthly delivery of multifile SDI results
NEWS 27 Mar 20
                 EVENTLINE will be removed from STN
NEWS 28 Mar 24
                 PATDPAFULL now available on STN
NEWS 29
        Mar 24
                 Additional information for trade-named substances without
                 structures available in REGISTRY
         Apr 11
NEWS 30
                .Display formats in DGENE enhanced
NEWS 31
         Apr 14
                MEDLINE Reload
NEWS 32
        Apr 17
                 Polymer searching in REGISTRY enhanced
NEWS 33
         Jun 13
                 Indexing from 1947 to 1956 added to records in CA/CAPLUS
NEWS 34
        Apr 21
                 New current-awareness alert (SDI) frequency in
                 WPIDS/WPINDEX/WPIX
NEWS 35
        Apr 28
                 RDISCLOSURE now available on STN
                 Pharmacokinetic information and systematic chemical names
NEWS 36
        May 05
                 added to PHAR
NEWS 37
         May 15
                 MEDLINE file segment of TOXCENTER reloaded
NEWS 38
         May 15
                 Supporter information for ENCOMPPAT and ENCOMPLIT updated
NEWS 39
         May 16
                 CHEMREACT will be removed from STN
        May 19 Simultaneous left and right truncation added to WSCA
NEWS 40
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10016280.1 Page 2

NEWS 41 May 19 RAPRA enhanced with new search field, simultaneous left and right truncation

NEWS 42 Jun 06 Simultaneous left and right truncation added to CBNB

NEWS 43 Jun 06 PASCAL enhanced with additional data

NEWS 44 Jun 20 2003 edition of the FSTA Thesaurus is now available

NEWS 45 Jun 25 HSDB has been reloaded

NEWS EXPRESS April 4 CURRENT WINDOWS VERSION IS V6.01a, CURRENT MACINTOSH VERSION IS V6.0b(ENG) AND V6.0Jb(JP), AND CURRENT DISCOVER FILE IS DATED 01 APRIL 2003

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FULL ESTIMATED COST

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TSCA INFORMATION NOW CURRENT THROUGH JANUARY 6, 2003

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Experimental and calculated property data are now available. See HELP PROPERTIES for more information. See STNote 27, Searching Properties in the CAS Registry File, for complete details: http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf

=>

10016280.1 Page 3

Uploading 10016280.1

STRUCTURE UPLOADED

=> d l1

L1 HAS NO ANSWERS

L1

STR

$$\begin{array}{c} \text{NH} \\ \text{NH} \\ \text{O} \\$$

Structure attributes must be viewed using STN Express query preparation.

=> s 11

SAMPLE SEARCH INITIATED 13:03:24 FILE 'REGISTRY' SAMPLE SCREEN SEARCH COMPLETED - 92 TO ITERATE

100.0% PROCESSED 92 ITERATIONS

G1 Cb,Cy,Hy,Ak

11 ANSWERS

SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE \*\*COMPLETE\*\*

BATCH \*\*COMPLETE\*\*

PROJECTED ITERATIONS:

1265 TO 2415

PROJECTED ANSWERS:

22 TO 418

L2

11 SEA SSS SAM L1

=> s l1 sss full

FULL SEARCH INITIATED 13:03:32 FILE 'REGISTRY' FULL SCREEN SEARCH COMPLETED - 1825 TO ITERATE

100.0% PROCESSED

1825 ITERATIONS

176 ANSWERS

SEARCH TIME: 00.00.01

176 SEA SSS FUL L1

=> file caplus

COST IN U.S. DOLLARS

SINCE FILE TOTAL

SESSION ENTRY

Patel

<6/302003>

FULL ESTIMATED COST

148.15 148.36

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FILE COVERS 1907 - 30 Jun 2003 VOL 139 ISS 1 FILE LAST UPDATED: 29 Jun 2003 (20030629/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> s 13 L4

L4 7 L3 .

=> d l4 fbib hitstr abs total

L4 ANSWER 1 OF 7 CAPLUS COPYRIGHT 2003 ACS

AN 2002:487536 CAPLUS

DN 137:63250

TI Quinazoline derivatives as inhibitors of human EFG tyrosine kinase

IN Himmelsbach, Frank; Langkopf, Elke; Blech, Stefan; Jung, Birgit; Baum, Elke; Solca, Flavio

PA Boehringer Ingelheim Pharma Kg, Germany

SO PCT Int. Appl., 64 pp. CODEN: PIXXD2

DT Patent

LA German

FAN CNT 1

PAN. CNI I																		
	PATENT NO.				KIND DATE				APPLICATION NO.						DATE			
ΡI	WO 20								WO 2001-EP14569					20011212				
	P.	: AE	, AG,	AL,	AM,	ΑT,	AU,	ΑZ,	BA,	BB,	BG,	BR,	BY,	ΒZ,	CA,	CH,	CN,	
			, CR,															
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		BF	, BJ,	CF,	CG,	CI,	CM,	GΑ,	GN,	GQ,	GW,	ML,	MR,	NE,	SN,	TD,	TG	
									DE 2000-10063435A 20001220									
	DE 10	DE 10063435 AU 2002019174			A1 200		0704		DE 2000-10063435 20001220									
	AU 20				A5 200		0701		AU 2002-19174 20011212									
									D	E 20	00-1	0063	435A	200	0122	0		

(prepn. of quinazoline derivs. as inhibitors of human EFG tyrosine kinase)

439081-40-0 CAPLUS RN

2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-[[(2S)-tetrahydro-2-CN furanyl]methoxy]-6-quinazolinyl]-4-(dimethylamino)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Double bond geometry unknown.

439081-48-8 CAPLUS RN

2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-CN 6-quinazolinyl]-4-[(2-methoxyethyl)methylamino]- (9CI) (CA INDEX NAME)

$$\begin{array}{c} & & & & \\ & & & \\ \text{MeO-CH}_2\text{-CH}_2\text{-CH} = \text{CH-C-NH} \\ & & & \\ \text{Me} & & \text{O} \end{array}$$

439081-20-6P 439081-21-7P 439081-22-8P 439081-24-0P 439081-25-1P 439081-27-3P 439081-28-4P 439081-31-9P 439081-32-0P 439081-36-4P 439081-37-5P 439081-38-6P

10016280.1

Page 6

439081-39-7P 439081-45-5P 439081-46-6P 439081-47-7P

RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(prepn. of quinazoline derivs. as inhibitors of human EFG tyrosine kinase)

RN 439081-20-6 CAPLUS

CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-[(tetrahydro-2-furanyl)methoxy]-6-quinazolinyl]-4-(dimethylamino)- (9CI) (CA INDEX NAME)

RN 439081-21-7 CAPLUS

CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-[(tetrahydro-3-furanyl)methoxy]-6-quinazolinyl]-4-(dimethylamino)- (9CI) (CA INDEX NAME)

RN 439081-22-8 CAPLUS

CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-[(tetrahydro-3-furanyl)methoxy]-6-quinazolinyl]-4-(diethylamino)- (9CI) (CA INDEX NAME)

RN 439081-24-0 CAPLUS

CN 2-Butenamide, 4-[bis(2-methoxyethyl)amino]-N-[4-[(3-chloro-4-fluorophenyl)amino]-7-[(tetrahydro-2-furanyl)methoxy]-6-quinazolinyl]-(9CI) (CA INDEX NAME)

RN 439081-25-1 CAPLUS

CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-[(tetrahydro-2-furanyl)methoxy]-6-quinazolinyl]-4-(4-morpholinyl)- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & & & \\ &$$

10016280.1

Page 8

RN 439081-27-3 CAPLUS

CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-[methyl[[(2R)-tetrahydro-2-furanyl]methyl]amino]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry unknown.

RN 439081-28-4 CAPLUS

CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-[methyl[[(2S)-tetrahydro-2-furanyl]methyl]amino]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Double bond geometry unknown.

RN 439081-31-9 CAPLUS

CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-(cyclopropylmethylamino)- (9CI) (CA INDEX NAME)

RN 439081-32-0 CAPLUS

CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-[methyl[(tetrahydro-2H-pyran-4-yl)methyl]amino]- (9CI) (CA INDEX NAME)

$$\begin{array}{c} \text{Me} \\ \text{CH}_2\text{-}\text{N} \\ \text{CH}_2\text{-}\text{N} \\ \text{CH}_2\text{-}\text{CH}_2\text{-}\text{CH} \\ \text{CH}_2\text{-}\text{NH} \\ \text{O} \\ \end{array}$$

RN 439081-36-4 CAPLUS

CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-[(tetrahydro-2H-pyran-4-yl)methoxy]-6-quinazolinyl]-4-(dimethylamino)- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & & & \\ & & & \\ \text{Me}_2\text{N}-\text{CH}_2-\text{CH} & \text{CH}-\text{C}-\text{NH} \\ & & & \\ \text{O} & & & \\ & & & \\ \end{array}$$

RN 439081-37-5 CAPLUS

CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-[(tetrahydro-2H-pyran-4-yl)methoxy]-6-quinazolinyl]-4-(4-morpholinyl)- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & & & \\ &$$

RN 439081-38-6 CAPLUS

CN 2-Butenamide, 4-[bis(2-methoxyethyl)amino]-N-[4-[(3-chloro-4-fluorophenyl)amino]-7-[(tetrahydro-2H-pyran-4-yl)methoxy]-6-quinazolinyl]-(9CI) (CA INDEX NAME)

$$\begin{array}{c} \text{MeO-CH}_2\text{-CH}_2 \\ \text{MeO-CH}_2\text{-CH}_2\text{-N-CH}_2\text{-CH-C-NH} \\ \text{O} \\ \end{array}$$

RN 439081-39-7 CAPLUS

CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-[[(2R)-tetrahydro-2-furanyl]methoxy]-6-quinazolinyl]-4-(dimethylamino)- (9CI) (CA INDEX NAME)

RN 439081-45-5 CAPLUS

CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-[[(2S)-tetrahydro-2-furanyl]methoxy]-6-quinazolinyl]-4-(ethylmethylamino)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry unknown.

RN 439081-46-6 CAPLUS

CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-[[(2S)-tetrahydro-2-furanyl]methoxy]-6-quinazolinyl]-4-(diethylamino)- (9CI) (CA INDEX NAME)

10016280.1

Page 12

RN 439081-47-7 CAPLUS

CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-[[(2S)-tetrahydro-2-furanyl]methoxy]-6-quinazolinyl]-4-[methyl(1-methylethyl)amino]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Double bond geometry unknown.

GI

AB Quinazoline derivs. I [R = PhCH2, PhCHMe, 3,4-Cl(F)C6H3; R1 = NMeR2, NEt2, NEtCH2CH2OMe, N(CH2CH2OMe)2, morpholino; R2 = Me, Et, CHMe2, cyclopropyl, CH2CH2OMe, 3-tetrahydrofuryl, 2-tetrahydrofurylmethyl, 3-tetrahydrofurylmethyl, 4-tetrahydropyranyl, 4-tetrahydropyranylmethyl; R3 = cyclopropylmethoxy, cyclobutyloxy, cyclopentyloxy, 3-tetrahydrofuranyloxy, 2-tetrahydrofuranylmethoxy, 3-tetrahydrofuranylmethoxy, 4-tetrahydropyranyloxy, 4-tetrahydropyranylmethoxy] were prepd. for use as inhibitors of signal transduction caused by human EFG receptor tyrosine kinase. They are useful in the treatment of tumoral diseases, diseases of the lung and the respiratory tract, the gastrointestinal tract, and the gallbladder and bile ducts. Thus, the quinazoline II was prepd. by converting bromocrotonic acid to its chloride, and reaction with 4-[(3-chloro-4-fluorophenyl)amino]-6-amino-7-cyclopropylmethoxyquinazoline, followed by MeNHCH2CH2OMe. II had an IC50 against human EFG receptor kinase of 0.7 nM.

RE.CNT 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

Ι

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L4 ANSWER 2 OF 7 CAPLUS COPYRIGHT 2003 ACS
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AN 2002:171892 CAPLUS

DN 136:216762

TI Preparation of 4-amino-6-heterocyclylcarbonylaminoquinazolines as epidermal growth factor receptor signal transduction inhibitors

IN Himmelsbach, Frank; Langkopf, Elke; Jung, Birgit; Blech, Stefan; Solca, Flavio

PA Boehringer Ingelheim Pharma Kg, Germany

SO PCT Int. Appl., 53 pp. CODEN: PIXXD2

DT Patent

LA German

FAN.CNT 1

PATENT NO. KIND DATE APPLICATION NO. DATE

PI WO 2002018376 A1 20020307 WO 2001-EP9536 20010818

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,

OS

IT

RN

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LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL,
         PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG,
         US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
    RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
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                                            DE 2000-10042062A 20000826
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MARPAT 136:216762
402569-98-6P 402569-99-7P 402570-00-7P
402570-01-8P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU
(Therapeutic use); BIOL (Biological study); PREP (Preparation); USES
(Uses)
```

CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-[(2R)-2-(methoxymethyl)-6-oxo-4-morpholinyl]- (9CI) (CA INDEX NAME)

growth factor receptor signal transduction inhibitors)

(prepn. of (amino) (heterocyclylcarbonylamino) quinazolines as epidermal

Absolute stereochemistry.

Double bond geometry unknown.

402569-98-6 CAPLUS

RN 402569-99-7 CAPLUS
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)6-quinazolinyl]-4-(2-oxo-1,9-dioxa-4-azaspiro[5.5]undec-4-yl)- (9CI) (CA
INDEX NAME)

Patel

$$\begin{array}{c|c} & & & & \\ & &$$

RN 402570-00-7 CAPLUS

CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-[(2S)-2-(methoxymethyl)-6-oxo-4-morpholinyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry unknown.

RN 402570-01-8 CAPLUS

CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-[2-(2-methoxyethyl)-6-oxo-4-morpholinyl]- (9CI) (CA INDEX NAME)

IT 402569-87-3P 402569-89-5P 402569-90-8P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(prepn. of (amino) (heterocyclylcarbonylamino) quinazolines as epidermal growth factor receptor signal transduction inhibitors)

RN 402569-87-3 CAPLUS

CN Glycine, N-[4-[[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]amino]-4-oxo-2-butenyl]-N-[(2R)-2-hydroxy-3-methoxypropyl]-, ethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.

RN 402569-89-5 CAPLUS

CN Glycine, N-[4-[[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]amino]-4-oxo-2-butenyl]-N-[(tetrahydro-4-hydroxy-2H-pyran-4-yl)methyl]-, ethyl ester (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & \\ & & & \\ &$$

RN 402569-90-8 CAPLUS

CN Glycine, N-[4-[[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]amino]-4-oxo-2-butenyl]-N-[(2S)-2-hydroxy-3-methoxypropyl]-, ethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry unknown.

GI

```
AΒ
     Title compds. [I; X = N, (substituted) methynyl; R1 = H, Me; R2 =
     (substituted) Ph, PhCH2, 1-phenylethyl; R3 = H, Me; A = (substituted)
     vinyl, ethynyl, 1,3-butadien-1,4-yl; B = (substituted) alkenyl,
     alkenylcarbonyl, etc.; C = (substituted) 2-oxomorpholin-4-yl, etc; D =
     oxyalkenyl, O; E = (substituted) amino, alkenylimino, imidazolyl,
     cycloalkyl; or DE = H, (substituted) alkoxy, etc.], were prepd. Thus,
     4-[(3-chloro-4-fluorophenyl)amino]-6-[(4-[N-(ethoxycarbonylmethyl)-N-((R)-
     2-hydroxy-3-methoxypropyl)amino]-1-oxo-2-buten-1-yl)amino]-7-
     cyclopropylmethoxyquinazoline (prepn. given) and MeSO2OH in MeCN were
     stirred for 4 h under reflux to give 69% 4-[(3-chloro-4-
     fluorophenyl)amino]-6-[(4-[(R)-2-methoxymethyl-6-oxomorpholin-4-yl]-1-oxo-
     2-buten-1-yl)amino]-7-cyclopropylmethoxyquinazoline. The latter inhibited
     epidermal growth factor (EGF)-dependent proliferation of F/L-HERc cells
     with IC50 = 2 nM. The invention relates to the use of the title compds.
     for treating tumor diseases, and lung and respiratory tract disorders.
RE.CNT 5
             THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD
             ALL CITATIONS AVAILABLE IN THE RE FORMAT
L4
     ANSWER 3 OF 7 CAPLUS COPYRIGHT 2003 ACS
ΑN
     2002:171889 CAPLUS
DN
     136:232315
ΤI
     Preparation of 4-amino-6-vinylcarbonylaminoquinazolines as epidermal
     growth factor receptor signal transduction inhibitors
     Himmelsbach, Frank; Langkopf, Elke; Jung, Birgit; Blech, Stefan; Solca,
IN
PA
     Boehringer Ingelheim Pharma Kg, Germany
SO
     PCT Int. Appl., 78 pp.
     CODEN: PIXXD2
DT
     Patent
LΑ
     German
FAN.CNT 1
     PATENT NO.
                     KIND DATE
                                          APPLICATION NO.
                                                            DATE
                           _____
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PΤ
     WO 2002018373
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             GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
             LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL,
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         RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,
             DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF,
             BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
                                           DE 2000-10042060A 20000826
     DE 10042060
                       Α1
                            20020307
                                           DE 2000-10042060 20000826
     US 2002077330
                       Α1
                            20020620
                                           US 2001-929931
                                                            20010815
                                           DE 2000-10042060A 20000826
                                           US 2000-230389PP 20000906
    AU 2001084021
                       A5
                            20020313
                                           AU 2001-84021
                                                            20010818
                                           DE 2000-10042060A 20000826
                                           WO 2001-EP9537 W 20010818
     EP 1315717
                            20030604
                      Α1
                                           EP 2001-962953
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             IE, SI, LT, LV, FI, RO, MK, CY, AL, TR
                                           DE 2000-10042060A 20000826
                                           WO 2001-EP9537 W 200.10818
OS
    MARPAT 136:232315
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## IT 402855-15-6P 402855-53-2P

RL: PAC (Pharmacological activity); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)

(prepn. of (amino) (vinylcarbonylamino) quinazolines as epidermal growth factor receptor signal transduction inhibitors)

RN 402855-15-6 CAPLUS

CN Glycine, N-[4-[[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]amino]-4-oxo-2-butenyl]-N-[(2S)-2-hydroxypropyl]-,
1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry unknown.

RN 402855-53-2 CAPLUS

CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-[(2R)-2-methyl-6-oxo-4-morpholinyl]- (9CI) (CA INDEX NAME)

IT 402855-16-7P 402855-17-8P 402855-18-9P 402855-19-0P 402855-33-8P 402855-35-0P 402855-46-3P 402855-47-4P 402855-48-5P 402855-49-6P 402855-51-0P 402855-52-1P 402855-54-3P 402855-70-3P 402855-71-4P 402855-73-6P 402855-74-7P 402855-75-8P 402855-76-9P 402855-77-0P RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses) (prepn. of (amino) (vinylcarbonylamino) quinazolines as epidermal growth factor receptor signal transduction inhibitors) RN 402855-16-7 CAPLUS CN Glycine, N-[4-[[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]amino]-4-oxo-2-butenyl]-N-[(2R)-2-hydroxypropyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry unknown.

RN 402855-17-8 CAPLUS

CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-[(1,3-dioxolan-2-ylmethyl)methylamino]- (9CI) (CA INDEX NAME)

RN 402855-18-9 CAPLUS
CN L-Alanine, N-[4-[[4-[(3-chloro-4-fluorophenyl)amino]-7(cyclopropylmethoxy)-6-quinazolinyl]amino]-4-oxo-2-butenyl]-N-(2hydroxyethyl)-, ethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry unknown.

RN 402855-19-0 CAPLUS
CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(2-methoxyethoxy)-6-quinazolinyl]-4-(5,5-dimethyl-2-oxo-4-morpholinyl)- (9CI) (CA INDEX NAME)

RN 402855-33-8 CAPLUS

CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-[(tetrahydro-2-furanyl)methoxy]-6-quinazolinyl]-4-(5,5-dimethyl-2-oxo-4-morpholinyl)-(9CI) (CA INDEX NAME)

RN 402855-35-0 CAPLUS

CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-(5-ethyl-2-oxo-4-morpholinyl)- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} \text{Et} & & & \\ & \text{CH}_2\text{-}\text{O} & & \\ & \text{N}\text{--}\text{CH}_2\text{--}\text{CH}\text{--}\text{CH}\text{--}\text{C-NH}\text{--}\text{N} \\ & \text{O} & & \text{NH} \\ & & \text{O} & & \\ & & \text{C1} & & \\ & & \text{F} & & \\ \end{array}$$

RN 402855-46-3 CAPLUS

CN Glycine, N-[4-[[4-[(3-chloro-4-fluorophenyl)amino]-7-[(tetrahydro-3-furanyl)methoxy]-6-quinazolinyl]amino]-4-oxo-2-butenyl]-N-[(2R)-2-hydroxypropyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry unknown.

RN 402855-47-4 CAPLUS

CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-[(tetrahydro-3-furanyl)methoxy]-6-quinazolinyl]-4-(2,2-dimethyl-6-oxo-4-morpholinyl)-(9CI) (CA INDEX NAME)

10016280.1

Page 24

RN 402855-48-5 CAPLUS

CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-[(tetrahydro-3-furanyl)methoxy]-6-quinazolinyl]-4-(5,5-dimethyl-2-oxo-4-morpholinyl)-(9CI) (CA INDEX NAME)

$$\begin{array}{c} \text{Me} \quad \text{Me} \\ \text{N---} \quad \text{CH}_2\text{---} \quad \text{CH}_2\text{---} \quad \text{CH}_2\text{---} \quad \text{NH} \\ \text{O} \\ \text{O} \\ \end{array}$$

RN 402855-49-6 CAPLUS

CN Glycine, N-[4-[[4-[(3-chloro-4-fluorophenyl)amino]-7-[(tetrahydro-2H-pyran-4-yl)methoxy]-6-quinazolinyl]amino]-4-oxo-2-butenyl]-N-[(2R)-2-hydroxypropyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

RN 402855-51-0 CAPLUS

CN Glycine, N-[4-[[4-[(3-chloro-4-fluorophenyl)amino]-7-[(tetrahydro-2H-pyran-4-yl)methoxy]-6-quinazolinyl]amino]-4-oxo-2-butenyl]-N-[(2S)-2-hydroxypropyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry unknown.

RN 402855-52-1 CAPLUS

CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-[(2S)-2-methyl-6-oxo-4-morpholinyl]- (9CI) (CA INDEX NAME)

RN 402855-54-3 CAPLUS

CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-[(3S)-3-methyl-2-oxo-4-morpholinyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry unknown.

RN 402855-70-3 CAPLUS

CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-[(tetrahydro-3-furanyl)methoxy]-6-quinazolinyl]-4-[(2R)-2-methyl-6-oxo-4-morpholinyl]-(9CI) (CA INDEX NAME)

RN 402855-71-4 CAPLUS

CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-[(tetrahydro-2H-pyran-4-yl)methoxy]-6-quinazolinyl]-4-[(2R)-2-methyl-6-oxo-4-morpholinyl]-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Double bond geometry unknown.

RN 402855-73-6 CAPLUS

CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-[(tetrahydro-2H-pyran-4-yl)methoxy]-6-quinazolinyl]-4-[(2S)-2-methyl-6-oxo-4-morpholinyl]-(9CI) (CA INDEX NAME)

RN 402855-74-7 CAPLUS

CN Glycine, N-[4-[[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]amino]-4-oxo-2-butenyl]-N-[(2R)-2-hydroxypropyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry unknown.

$$\bigcap_{Me} \bigcap_{R} \bigcap_{N} \bigcap_{R} \bigcap_{R} \bigcap_{N} \bigcap_{R} \bigcap_{$$

RN 402855-75-8 CAPLUS

CN Glycine, N-[4-[[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]amino]-4-oxo-2-butenyl]-N-(2-hydroxy-2-methylpropyl)- (9CI) (CA INDEX NAME)

RN 402855-76-9 CAPLUS

CN Glycine, N-[4-[[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]amino]-4-oxo-2-butenyl]-N-(2-hydroxy-1,1-dimethylethyl)-(9CI) (CA INDEX NAME)

$$\begin{array}{c} \text{HO}_2\text{C}-\text{CH}_2\\ \text{Me}\\ \text{HO}-\text{CH}_2-\text{C}-\text{N}-\text{CH}_2-\text{CH}-\text{C}-\text{NH}\\ \text{Me} \\ \end{array} \begin{array}{c} \text{CH}_2-\text{O}\\ \text{NH}\\ \text{O} \\ \end{array}$$

RN 402855-77-0 CAPLUS

CN Glycine, N-[4-[[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]amino]-4-oxo-2-butenyl]-N-[(2R)-2-hydroxypropyl]-, methyl ester (9CI) (CA INDEX NAME)

GI

NHR1  
NH-CO-CH=CH
$$\left\{CH_{2}\right\}$$
R2  
n

AB Title compds. [I; R1 = PhCH2, 1-phenylethyl, (substituted) Ph; R2 = N-[(1,3-dioxolan-2-yl)methyl]methylamino, (substituted) R4OCOCH2NCH2CH2OH, 2-oxomorpholin-4-yl; R4 = H, alkyl; R3 = H, (alkoxy)alkoxy, cycloalkylalkoxy, tetrahydrofuran-3-yloxy, tetrahydropyran-3-yloxy, tetrahydropyran-4-yloxy, tetrahydrofuranylmethoxy, tetrahydropyranylmethoxy; n = 1-3], were prepd. Thus, a mixt. of 6-amino-4-[(3-chloro-4-fluorophenyl)amino]-7-cyclopropylmethoxyquinazoline (prepn. given) and disopropylethylamine in THF was dropwise treated under ice-cooling with BrCH2CH: CHCO2Cl (prepn. given) in CH2Cl2 followed by stirring for 1 h under ice-cooling and for 2 h at room temp. and addn. of (S)-(2-hydroxypropylamino)acetic acid tert-Bu ester in CH2Cl2 to give after stirring over night at room temp. and stirring for 5 h at 60.degree. 64% 4-[(3-chloro-4-fluorophenyl)amino]-6-[(4-[N-(tertbutyloxycarbonylmethyl)-N-((S)-2-hydroxyprop-1-yl)amino]-1-oxo-2-buten-1yl)amino]-7-cyclopropylmethoxyquinazoline. Several I inhibited epidermal growth factor (EGF)-dependent proliferation of F/L-HERc cells with IC50 = 0.02-15~nM. The invention relates to the use of the title compds. for treating tumor diseases, and lung and respiratory tract disorders. RE.CNT 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD

L4 ANSWER 4 OF 7 CAPLUS COPYRIGHT 2003 ACS

AN 2001:762992 CAPLUS

DN 135:303907

TI Preparation of quinazolines as inhibitors of epidermal growth

ALL CITATIONS AVAILABLE IN THE RE FORMAT

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factor-mediated signal transduction.
     Himmelsbach, Frank; Langkopf, Elke; Jung, Birgit; Blech, Stefan; Solca,
IN
PA
     Boehringer Ingelheim Pharma K.-G., Germany
SO
     PCT Int. Appl., 95 pp.
     CODEN: PIXXD2
DT
     Patent
LΑ
     German
FAN.CNT 2
     PATENT NO.
                        KIND DATE
                                                 APPLICATION NO.
                                                 -----
     WO 2001077104
PΙ
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                                               WO 2001-EP3694 20010331
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              HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS,
              LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO,
              RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ,
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                                                 DE 2000-10017539A 20000408
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                         A1
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                         Α1
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                                                 DE 2000-10040525A 20000818
                                                 WO 2001-EP3694 W 20010331
PATENT FAMILY INFORMATION:
FAN
    2001:747043
     PATENT NO.
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                               DATE
                                                APPLICATION NO. DATE
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ΡI
     DE 10017539
                         Α1
                                20011011
                                                 DE 2000-10017539 20000408
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                         A1
                                20011122
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     WO 2001077104
                               20011018
                        A1
                                                 WO 2001-EP3694 20010331
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              DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF,
              BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
                                                 DE 2000-10017539A 20000408
                                                 DE 2000-10040525A 20000818
     EP 1280798
                               20030205
                         Α1
                                                 EP 2001-938076 20010331
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              IE, SI, LT, LV, FI, RO, MK, CY, AL, TR
                                                 DE 2000-10017539A 20000408
                                                 DE 2000-10040525A 20000818
                                                 WO 2001-EP3694 W 20010331
OS
     MARPAT 135:303907
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ΙT 365532-35-0P 365532-36-1P 365532-37-2P 365532-39-4P 365532-40-7P 365532-41-8P 365532-42-9P 365532-44-1P 365532-45-2P 365532-46-3P 365532-47-4P 365532-48-5P 365532-49-6P 367282-07-3P 367282-12-0P 367282-15-3P 367282-23-3P 367282-25-5P 367282-27-7P 367282-29-9P RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses) (prepn. of quinazolines as inhibitors of epidermal growth factor-mediated signal transduction) RN 365532-35-0 CAPLUS CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-[4-(tetrahydro-2-oxo-3-furanyl)-1-piperazinyl]- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & & & \\ &$$

RN 365532-36-1 CAPLUS

CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-[4-[(2R)-tetrahydro-5-oxo-2-furanyl]methyl]-1-piperazinyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry unknown.

$$\bigcap_{\mathbb{R}} \bigcap_{\mathbb{N}} \bigcap$$

Patel

RN 365532-37-2 CAPLUS

CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-[4-[methyl(tetrahydro-2-oxo-3-furanyl)amino]-1-piperidinyl]- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & & & \\ &$$

RN 365532-39-4 CAPLUS

CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-[4-(tetrahydro-5-oxo-3-furanyl)-1-piperazinyl]- (9CI) (CA INDEX NAME)

$$\begin{array}{c} & & & \\ & &$$

RN 365532-40-7 CAPLUS

CN 2-Propenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-3-[1-(tetrahydro-5-oxo-3-furanyl)-4-piperidinyl]- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & & & \\ &$$

RN 365532-41-8 CAPLUS

CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-[4-[(2S)-tetrahydro-5-oxo-2-furanyl]carbonyl]-1-piperazinyl]- (9CI) (CA INDEX NAME)

RN 365532-42-9 CAPLUS

CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-[4-[2-[(tetrahydro-2-oxo-3-furanyl)thio]ethyl]-1-piperazinyl]- (9CI) (CA INDEX NAME)

RN 365532-44-1 CAPLUS

CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-(3-oxo-2-oxa-8-azaspiro[4.5]dec-8-yl)- (9CI) (CA INDEX NAME)

RN 365532-45-2 CAPLUS

CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-(hexahydro-3-oxopyrazino[2,1-c][1,4]oxazin-8(1H)-yl)-(9CI) (CA INDEX NAME)

$$\begin{array}{c|c} C1 & F \\ \hline \\ O & N \\ \hline \\ O & N \\ \hline \\ CH_2-CH \\ \hline \\ CH_2-O \\ \hline \\ \end{array}$$

RN 365532-46-3 CAPLUS

CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-(1-oxo-2-oxa-8-azaspiro[4.5]dec-8-yl)- (9CI) (CA INDEX NAME)

RN 365532-47-4 CAPLUS

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CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-(hexahydro-1-oxopyrazino[2,1-c][1,4]oxazin-8(1H)-yl)-(9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & &$$

RN 365532-48-5 CAPLUS

CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-[4-[(tetrahydro-2-oxo-3-furanyl)thio]-1-piperidinyl]-(9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & & & \\ &$$

RN 365532-49-6 CAPLUS

CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-[4-[(2,2-dimethyl-6-oxo-4-morpholinyl)methyl]-1-piperidinyl]- (9CI) (CA INDEX NAME)

Me 
$$\sim$$
 CH<sub>2</sub>  $\sim$  CH<sub>2</sub>  $\sim$  CH<sub>2</sub>  $\sim$  CH<sub>2</sub>  $\sim$  NH  $\sim$  NH  $\sim$  NH  $\sim$  CH<sub>2</sub>  $\sim$  CH<sub>2</sub>  $\sim$  NH  $\sim$  NH  $\sim$  CH<sub>2</sub>  $\sim$  NH  $\sim$  NH  $\sim$  CH<sub>2</sub>  $\sim$  NH  $\sim$  NH  $\sim$  NH  $\sim$  CH<sub>2</sub>  $\sim$  NH  $\sim$  NH  $\sim$  NH  $\sim$  NH  $\sim$  CH<sub>2</sub>  $\sim$  NH  $\sim$ 

RN 367282-07-3 CAPLUS

CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-[methyl[1-(tetrahydro-2-oxo-3-furanyl)-4-piperidinyl]amino]- (9CI) (CA INDEX NAME)

$$\begin{array}{c} \text{Me} \\ \text{N-CH}_2\text{-CH} \\ \text{CH-C-NH} \\ \text{O} \\ \text{NH} \\ \text{C1} \\ \text{F} \end{array}$$

RN 367282-12-0 CAPLUS

CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-[methyl[1-[[(2S)-tetrahydro-5-oxo-2-furanyl]carbonyl]-4-piperidinyl]amino]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.

PAGE 1-A

PAGE 1-B

RN

367282-15-3 CAPLUS
2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-[1-(tetrahydro-2-oxo-3-furanyl)-4-piperidinyl]- (9CI)
(CA INDEX NAME) CN

Patel

<6/302003>

$$\begin{array}{c|c} & & & \\ &$$

RN 367282-23-3 CAPLUS

CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-[4-(2-oxo-4-morpholinyl)-1-piperidinyl]- (9CI) (CA INDEX NAME)

RN 367282-25-5 CAPLUS

CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-[4-[(2R)-2-methyl-6-oxo-4-morpholinyl]-1-piperidinyl]-(9CI) (CA INDEX NAME)

Absolute stereochemistry. Double bond geometry unknown.

Page 41

RN 367282-27-7 CAPLUS

CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-(4-methyl-2-oxo-1-oxa-4,9-diazaspiro[5.5]undec-9-yl)-(9CI) (CA INDEX NAME)

RN 367282-29-9 CAPLUS

CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-(2-oxo-3-oxa-9-azaspiro[5.5]undec-9-yl)- (9CI) (CA INDEX NAME)

IT 367283-05-4 367283-07-6

RL: RCT (Reactant); RACT (Reactant or reagent) (prepn. of quinazolines as inhibitors of epidermal growth factor-mediated signal transduction)

RN 367283-05-4 CAPLUS

CN Glycine, N-[1-[4-[[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]amino]-4-oxo-2-butenyl]-4-piperidinyl]-N-(2-hydroxyethyl)-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

RN 367283-07-6 CAPLUS

CN Glycine, N-[1-[4-[[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]amino]-4-oxo-2-butenyl]-4-piperidinyl]-N-[(2R)-2-hydroxypropyl]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry unknown.

$$\begin{array}{c|c} & & & \\ & & \\ & & \\ N \\ & & \\ N \\ & \\ CH_2 \\ & \\ NH_1 \\ & \\ NH_2 \\ & \\ C1 \\ & \\ F \end{array}$$

RN 290304-01-7 CAPLUS 

CN 1-Piperazinecarboxylic acid, 4-[4-[[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]amino]-4-oxo-2-butenyl]-,
1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & & & \\ &$$

RN 365532-06-5 CAPLUS

CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-[4-(methylamino)-1-piperidinyl]- (9CI) (CA INDEX NAME)

MeNH 
$$CH_2-CH=CH-C-NH$$
 $CH_2-CH=CH-C-NH$ 
 $CH_2-CH=CH-C-NH$ 
 $CH_2-CH=CH-C-NH$ 
 $CH_2-CH=CH-C-NH$ 
 $CH_2-CH=CH-C-NH$ 

RN 365532-07-6 CAPLUS

CN 2-Propenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-3-(4-piperidinyl)- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & & & \\ &$$

RN 365532-18-9 CAPLUS

CN Carbamic acid, [1-[4-[[4-[(3-chloro-4-fluorophenyl)amino]-7-

Page 45

(cyclopropylmethoxy)-6-quinazolinyl]amino]-4-oxo-2-butenyl]-4piperidinyl]methyl-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

t-BuO-C-N 
$$\begin{array}{c|c} O & Me \\ \hline \\ N-CH_2-CH=CH-C-NH \\ \hline \\ O \\ \end{array}$$

RN 365532-19-0 CAPLUS

CN 1-Piperidinecarboxylic acid, 4-[3-[[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]amino]-3-oxo-1-propenyl]-,
1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

RN 367282-36-8 CAPLUS

CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-(methyl-4-piperidinylamino)- (9CI) (CA INDEX NAME)

$$\begin{array}{c} \text{Me} \\ \text{N-CH}_2\text{-CH} = \text{CH-C-NH} \\ \text{O} \\ \end{array}$$

RN 367282-44-8 CAPLUS

CN 1-Piperidinecarboxylic acid, 4-[[4-[[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]amino]-4-oxo-2-butenyl]methylamino]-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

GΙ

Title compds. [I; X = NCN, N; R1 = H, alkyl; R2 = (substituted) Ph, PhCH2, PhCH2CH2; R3 = H, alkyl; R4 = H, alkoxy, cycloalkoxy, cycloalkylalkoxy; A = (substituted) vinylene; B = bond, (fluoro)alkylene; D = substituted pyrrolidinyl, piperidinyl, piperazinyl, etc.], were prepd. Thus, 4-[(3-chloro-4-fluorophenyl)amino]-6-[[4-(piperazin-1-yl)-1-oxo-2-buten-1-yl]amino]-7-cyclopropylmethoxyquinazoline (prepn. given) in THF was

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Page 47
     treated with Et3N and then with 3-bromodihydrofuran-2-one in THF under ice
     cooling followed by stirring for 48 h at room temp. to give 56%
     4-[(3-chloro-4-fluorophenyl)amino]-6-[[4-[4-(2-oxotetrahydrofuran-3-
    yl)piperazin-1-yl]-1-oxo-2-buten-1-yl]amino]-7-
     cyclopropylmethoxyquinazoline. The latter inhibited epidermal growth
     factor (EGF)-dependent proliferation of F/L-HERC cells with IC50 = 0.05
    nM.
RE.CNT 5
             THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD
             ALL CITATIONS AVAILABLE IN THE RE FORMAT
    ANSWER 5 OF 7 CAPLUS COPYRIGHT 2003 ACS
     2001:747043 CAPLUS
     135:303901
    Bicyclic heterocycles as inhibitors of epidermal growth factor receptor
     mediated signal transduction
    Himmelsbach, Frank; Langkopf, Elke; Jung, Birgit; Blech, Stefan; Solca,
     Flavio
```

PA Boehringer Ingelheim Pharma KG, Germany

SO Ger. Offen., 28 pp.

CODEN: GWXXBX

DT Patent

German LΑ

FAN.CNT 2

T.4

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DN

TΙ

IN

	PATENT NO.	KIND DATE	APPLICATION NO. DATE						
PI	DE 10017539 US 2001044435		US 2001-816003 20010323 DE 2000-10017539A 20000408						
	WO 2001077104	A1 20011018	DE 2000-10040525A 20000818 WO 2001-EP3694 20010331						
	W: AE, AG, CO, CR, HR, HU, LT, LU, RU, SD, VN, YU, RW: GH, GM, DE, DK,	AL, AM, AT, AU, CU, CZ, DE, DK, ID, IL, IN, IS, LV, MA, MD, MG, SE, SG, SI, SK, ZA, ZW, AM, AZ, KE, LS, MW, MZ, ES, FI, FR, GB,	AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, BY, KG, KZ, MD, RU, TJ, TM SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, GN, GW, ML, MR, NE, SN, TD, TG						
	EP 1280798	A1 20030205	DE 2000-10040525A 20000818 EP 2001-938076 20010331						
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PATENT FAMILY INFORMATION:

FAN 2001:762992

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PATENT NO.
                     KIND DATE
                                         APPLICATION NO. DATE
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                                         -----
                          20011018
ΡI
    WO 2001077104
                     A1
                                        WO 2001-EP3694 20010331
        W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
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            HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS,
            LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO,
            RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ,
            VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
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## 10016280.1 Page 48

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG DE 2000-10017539A 20000408 DE 2000-10040525A 20000818 DE 10017539 Α1 20011011 DE 2000-10017539 20000408 DE 10040525 A1 20020228 DE 2000-10040525 20000818 EP 1280798 A1 20030205 EP 2001-938076 20010331 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR DE 2000-10017539A 20000408 DE 2000-10040525A 20000818 WO 2001-EP3694 W 20010331 MARPAT 135:303901

OS

IT 365532-35-0P 365532-39-4P 365532-42-9P 365532-45-2P 365532-47-4P 365532-48-5P 365532-49-6P

> RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(prepn. of bicyclic heterocycles as inhibitors of epidermal growth factor receptor mediated signal transduction)

RN 365532-35-0 CAPLUS

2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-CN 6-quinazolinyl]-4-[4-(tetrahydro-2-oxo-3-furanyl)-1-piperazinyl]- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & & & \\ &$$

RN 365532-39-4 CAPLUS

CN2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-[4-(tetrahydro-5-oxo-3-furanyl)-1-piperazinyl]- (9CI) (CA INDEX NAME)

RN 365532-42-9 CAPLUS

CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-[4-[2-[(tetrahydro-2-oxo-3-furanyl)thio]ethyl]-1-piperazinyl]- (9CI) (CA INDEX NAME)

RN 365532-45-2 CAPLUS

CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-(hexahydro-3-oxopyrazino[2,1-c][1,4]oxazin-8(1H)-yl)-(9CI) (CA INDEX NAME)

RN 365532-47-4 CAPLUS

Page 50

CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-(hexahydro-1-oxopyrazino[2,1-c][1,4]oxazin-8(1H)-yl)-(9CI) (CA INDEX NAME)

RN 365532-48-5 CAPLUS

CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-[4-[(tetrahydro-2-oxo-3-furanyl)thio]-1-piperidinyl]-(9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & & & \\ &$$

RN 365532-49-6 CAPLUS

CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-[4-[(2,2-dimethyl-6-oxo-4-morpholinyl)methyl]-1-piperidinyl]- (9CI) (CA INDEX NAME)

$$\begin{array}{c} \text{Me} \\ \text{Me} \\ \text{N} \\ \text{CH}_2 \\ \text{NH} \\ \text{NH} \\ \text{CH}_2 \\$$

$$\begin{array}{c|c} & & & \\ &$$

RN 290304-01-7 CAPLUS

CN 1-Piperazinecarboxylic acid, 4-[4-[[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]amino]-4-oxo-2-butenyl]-,

1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

RN 365532-06-5 CAPLUS

CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-[4-(methylamino)-1-piperidinyl]- (9CI) (CA INDEX NAME)

RN 365532-07-6 CAPLUS

CN 2-Propenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-3-(4-piperidinyl)- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & & & \\ & & \\ & & \\ \text{CH} & \text{CH} & \text{C} & \text{NH} \\ & & \\$$

RN 365532-10-1 CAPLUS

CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-

Patel

Page 53

6-quinazolinyl]-4-[1-(methylamino)-4-piperidinyl]- (9CI) (CA INDEX NAME)

$$\begin{array}{c} \begin{array}{c} \begin{array}{c} \\ \\ \\ \\ \end{array} \end{array} \begin{array}{c} \\ \\ \\ \end{array} \begin{array}{c} \\ \\ \\ \end{array} \begin{array}{c} \\ \\ \end{array} \begin{array}{c} \\ \\ \\$$

RN 365532-18-9 CAPLUS

CN Carbamic acid, [1-[4-[[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]amino]-4-oxo-2-butenyl]-4-piperidinyl]methyl-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

t-BuO-C-N 
$$\sim$$
 CH<sub>2</sub>-CH=CH-C-NH  $\sim$  NH  $\sim$  Cl

RN 365532-19-0 CAPLUS

CN 1-Piperidinecarboxylic acid, 4-[3-[[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]amino]-3-oxo-1-propenyl]-,
1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

Page 54

$$\begin{array}{c} \text{t-BuO-C} \\ \text{N} \\ \text{CH} \\ \text{CH} \\ \text{CH} \\ \text{C} \\ \text{N} \\ \text{N} \\ \text{N} \\ \text{C} \\ \text{I} \\ \text{F} \\ \end{array}$$

RN 365532-21-4 CAPLUS

CN Carbamic acid, [4-[4-[[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]amino]-4-oxo-2-butenyl]-1-piperidinyl]methyl-, 1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

t-BuO-C-N
$$CH_2-CH=CH-C-NH$$

$$CH_2-CH=CH-C-NH$$

$$CH_2-CH=CH-C-NH$$

$$CH_2-CH=CH-C-NH$$

IT 365532-36-1P 365532-37-2P 365532-38-3P
 365532-40-7P 365532-41-8P 365532-43-0P
 365532-44-1P 365532-46-3P
 RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(prepn. of bicyclic heterocycles as inhibitors of epidermal growth factor receptor mediated signal transduction)

RN 365532-36-1 CAPLUS

CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-[4-[((2R)-tetrahydro-5-oxo-2-furanyl]methyl]-1-piperazinyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Double bond geometry unknown.

RN 365532-37-2 CAPLUS

CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-[4-[methyl(tetrahydro-2-oxo-3-furanyl)amino]-1-piperidinyl]- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & & & \\ &$$

RN 365532-38-3 CAPLUS

CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-[1-[methyl(tetrahydro-2-oxo-3-furanyl)amino]-4-piperidinyl]- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & & & \\ &$$

RN 365532-40-7 CAPLUS

CN 2-Propenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-3-[1-(tetrahydro-5-oxo-3-furanyl)-4-piperidinyl]- (9CI) (CA INDEX NAME)

$$\begin{array}{c} \begin{array}{c} \begin{array}{c} \\ \\ \\ \\ \end{array} \end{array} \begin{array}{c} \\ \\ \\ \end{array} \begin{array}{c} \\ \\ \\ \end{array} \begin{array}{c} \\ \\ \end{array} \begin{array}{c} \\ \\ \\$$

RN 365532-41-8 CAPLUS

CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-[4-[(2S)-tetrahydro-5-oxo-2-furanyl]carbonyl]-1-piperazinyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Double bond geometry unknown.

RN 365532-43-0 CAPLUS

CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-[4-(tetrahydro-2-oxo-3-furanyl)-1-piperidinyl]- (9CI) (CA INDEX NAME)

RN 365532-44-1 CAPLUS

CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-(3-oxo-2-oxa-8-azaspiro[4.5]dec-8-yl)- (9CI) (CA INDEX NAME)

Page 58

RN 365532-46-3 CAPLUS

CN 2-Butenamide, N-'[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-(1-oxo-2-oxa-8-azaspiro[4.5]dec-8-yl)- (9CI) (CA INDEX NAME)

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Patel

AB Bicyclic heterocycles I [X = N, CCN; R = substituted NH2; R1 = H, alkyl; R2 = acyl; R3 = H, (un)substituted alkoxy, cycloalkoxy, tetrahydrofuranyloxy, tetrahydrofuranyloxy, tetrahydrofuranyloxy, tetrahydrofuranylmethoxy, tetrahydropyranylmethoxy] were prepd. for use as inhibitors of tyrosine kinase-mediated signal transduction for treatment of tumors and diseases of the lung and airway. Thus, 4-[(3-chloro-4-fluorophenyl)amino]-7-fluoro-6-nitroquinazoline was treated with cyclopropylmethanol, followed by redn. to the amine, reaction with 4-bromocrotonic acid and N-tert.-butoxycarbonylpiperazine, and deblocking to give the quinazoline II. II had an IC50 for inhibition of epidermal growth factor dependent proliferation of 0.05 nM.

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L4 ANSWER 6 OF 7 CAPLUS COPYRIGHT 2003 ACS
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AN 2000:911231 CAPLUS

DN 134:71599

- TI Preparation of aminoquinazolines and aminoquinolines as epidermal growth factor receptor signal transduction inhibitors.
- IN Himmelsbach, Frank; Langkopf, Elke; Metz, Thomas; Solca, Flavio; Jung, Birgit; Baum, Anke
- PA Boehringer Ingelheim Pharma K.-G., Germany

SO PCT Int. Appl., 104 pp.

CODEN: PIXXD2

DT Patent

LA German

FAN.CNT 1

	PATENT NO.			KI	ND :	DATE			A	PPLI	CATI	N NC	o. :	DATE				
		<b>-</b>					<del>-</del>		_									
ΡI	WO 2000078735			A	1 :	2000	1228		W	O 20	00-E	P554	7 :	2000	0616			
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US 1999-146644PP 19990730
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                                       DE 1999-19928281A 19990621
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                                      WO 2000-EP5547 W 20000616
JP 2003502410
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                                      NO 2001-6185
                                                       20011218
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314771-28-3P 314771-31-8P 314771-32-9P
314771-33-0P 314771-34-1P 314771-45-4P
314771-46-5P 314771-47-6P 314771-48-7P
314771-49-8P 314771-50-1P 314771-51-2P
314771-52-3P 314771-53-4P 314771-54-5P
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314771-62-5P 314771-63-6P 314771-64-7P
314771-65-8P 314771-67-0P 314771-68-1P
314771-69-2P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological
study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use);
BIOL (Biological study); PREP (Preparation); USES (Uses)
   (prepn. of aminoquinazolines and aminoquinolines as epidermal growth
   factor receptor signal transduction inhibitors)
314771-10-3 CAPLUS
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Page 61

CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-(dimethylamino)- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & & & \\ & & \\ \text{CH}_2 - \text{O} & & \\ & & \\ \text{Me}_2 \text{N} - \text{CH}_2 - \text{CH} = \text{CH} - \text{C} - \text{NH} \\ & & \\ \text{O} & & \\ & &$$

RN 314771-12-5 CAPLUS

CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-(4-piperidinyl)- (9CI) (CA INDEX NAME)

RN 314771-20-5 CAPLUS

CN 2-Butenamide, N-[4-[(3-bromophenyl)amino]-7-[(1-methyl-4-piperidinyl)methoxy]-6-quinazolinyl]- (9CI) (CA INDEX NAME)

Page 62

RN 314771-21-6 CAPLUS

CN 2-Butenoic acid, 4-[[4-[(3-bromophenyl)amino]-7-[3-(1-methyl-4-piperidinyl)propoxy]-6-quinazolinyl]amino]-4-oxo-, ethyl ester (9CI) (CAINDEX NAME)

Me N 
$$(CH_2)_3-0$$
 N N  $N$  EtO-C-CH  $CH$ -C-NH  $N$  NH

RN 314771-26-1 CAPLUS

CN 2,4-Hexadienamide, N-[4-[(3-bromophenyl)amino]-7-[3-(1-methyl-4-piperidinyl)propoxy]-6-quinazolinyl]- (9CI) (CA INDEX NAME)

RN 314771-27-2 CAPLUS

CN 2-Butenamide, N-[4-[(3-bromophenyl)amino]-7-[3-(1-methyl-4-piperidinyl)propoxy]-6-quinazolinyl]- (9CI) (CA INDEX NAME)

RN 314771-28-3 CAPLUS

CN 2-Propenamide, N-[4-[(3-bromophenyl)amino]-7-[3-(1-methyl-4-piperidinyl)propoxy]-6-quinazolinyl]-3-phenyl- (9CI) (CA INDEX NAME)

RN 314771-31-8 CAPLUS

CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-(4-morpholinyl)- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & & & \\ &$$

RN 314771-32-9 CAPLUS

CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-(4-ethyl-1-piperazinyl)- (9CI) (CA INDEX NAME)

Patel

$$\begin{array}{c|c} & & & \\ &$$

RN 314771-33-0 CAPLUS

CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-(2,6-dimethyl-4-morpholinyl)- (9CI) (CA INDEX NAME)

Me 
$$CH_2-CH=CH-C-NH$$
 $CH_2-CH=CH-C-NH$ 
 $CH_2-CH-C-NH$ 
 $CH_2-$ 

RN 314771-34-1 CAPLUS

CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-(1-oxido-4-thiomorpholinyl)- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & & & \\ &$$

10016280.1 Page 65

RN 314771-45-4 CAPLUS

CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-[methyl(1-methyl-4-piperidinyl)amino]- (9CI) (CA INDEX NAME)

RN 314771-46-5 CAPLUS

CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-[(2R)-2-(methoxymethyl)-1-pyrrolidinyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Double bond geometry unknown.

RN 314771-47-6 CAPLUS

CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-[(2S)-2-(methoxymethyl)-1-pyrrolidinyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Double bond geometry unknown.

RN 314771-48-7 CAPLUS

CN 2-Butenamide, 4-[bis(2-methoxyethyl)amino]-N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]- (9CI) (CAINDEX NAME)

RN 314771-49-8 CAPLUS

CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-[ethyl(2-methoxyethyl)amino]-(9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & & & \\ & & & \\ \text{MeO-CH}_2\text{-CH}_2\text{-N-CH}_2\text{-CH} \\ & & & \\ \text{Et} & & \text{O} \end{array}$$

RN 314771-50-1 CAPLUS

CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-(1-piperidinyl)- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & & & \\ & & \\ & & \\ N - CH_2 - CH - C - NH - CH_2 - CH_2$$

RN 314771-51-2 CAPLUS

CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-(2-methyl-1-piperidinyl)- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & & & \\ & & \\ & & \\ N & \\ \text{CH}_2 - \text{CH} = \text{CH} - \text{C} - \text{NH} \\ & & \\ \text{NH} & & \\ &$$

RN 314771-52-3 CAPLUS

CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-(1-pyrrolidinyl)- (9CI) (CA INDEX NAME)

Patel

$$\begin{array}{c|c} & & & \\ & & \\ N - CH_2 - CH - C - NH - CH_2 - CH_$$

RN 314771-53-4 CAPLUS

CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-[4-(cyclopropylmethyl)-1-piperazinyl]- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & & & \\ &$$

RN 314771-54-5 CAPLUS

CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-(2-methyl-1-pyrrolidinyl)- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} \text{Me} & & & \\ & \text{CH}_2\text{-O} & & \\ \text{N-CH}_2\text{-CH} & \text{CH-C-NH} & \\ \text{O} & & & \\ & \text{NH} & \\ & & & \\ \end{array}$$

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RN 314771-55-6 CAPLUS

CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-[methyl(tetrahydro-2H-pyran-4-yl)amino]- (9CI) (CA INDEX NAME)

$$\begin{array}{c} \text{Me} \\ \text{N-CH}_2\text{-CH} = \text{CH-C-NH} \\ \text{N} \\ \text{Cl} \\ \text{F} \end{array}$$

RN 314771-56-7 CAPLUS

CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-[(2R,6S)-2,6-dimethyl-1-piperidinyl]-, rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.

Double bond geometry unknown.

RN 314771-57-8 CAPLUS

CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-(2,5-dimethyl-1-pyrrolidinyl)- (9CI) (CA INDEX NAME)

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RN 314771-58-9 CAPLUS

CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-[(tetrahydro-2-furanyl)methoxy]-6-quinazolinyl]-4-(diethylamino)- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} C & CH_2 - O & N \\ \hline \\ Et_2N - CH_2 - CH - C - NH & NH \\ \hline \\ O & NH \\ \hline \\ C1 & F \\ \end{array}$$

RN 314771-60-3 CAPLUS

CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-[4-[(diethylamino)methyl]-1-piperidinyl]- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & & & \\ & & \\ & & \\ \text{CH}_2 - \text{O} \\ & & \\ \text{NH} \\ & & \\ \text{C1} \\ & &$$

RN 314771-61-4 CAPLUS

CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-

Patel

Page 71

6-quinazolinyl]-4-[(cyclopropylmethyl)methylamino]- (9CI) (CA INDEX NAME)

$$\begin{array}{c} \text{Me} \\ \text{CH}_2\text{-N-CH}_2\text{-CH} \\ \text{CH}_2\text{-N-CH}_2\text{-CH} \\ \text{CH}_2\text{-N-CH}_2\text{-CH} \\ \text{CH}_2\text{-N-CH}_2\text{-CH} \\ \text{CH}_2\text{-N-CH}_2\text{-CH} \\ \text{CH}_2\text{-N-CH}_2\text{-CH} \\ \text{CH}_2\text{-N-CH}_2\text{$$

RN 314771-62-5 CAPLUS

CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-[(2-methoxycyclopropyl)methylamino]- (9CI) (CA INDEX NAME)

RN 314771-63-6 CAPLUS

CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-[(3-methoxypropyl)methylamino]- (9CI) (CA INDEX NAME)

MeO- (CH<sub>2</sub>)<sub>3</sub>-N-CH<sub>2</sub>-CH=CH-C-NH

Me

O

$$\begin{array}{c}
CH_2-O\\
CH_$$

Patel

Page 72

RN 314771-64-7 CAPLUS

CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-(4-methoxy-1-piperidinyl)- (9CI) (CA INDEX NAME)

$$\begin{array}{c} & & & \\ & &$$

RN 314771-65-8 CAPLUS

CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-(4-hydroxy-1-piperidinyl)- (9CI) (CA INDEX NAME)

RN 314771-67-0 CAPLUS

CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-[methyl[(tetrahydro-2-furanyl)methyl]amino]- (9CI) (CA INDEX NAME)

RN 314771-68-1 CAPLUS

CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-[methyl(tetrahydro-3-furanyl)amino]- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & & & \\ & & \\ N-CH_2-CH-C-NH \\ & & \\ NH \\ & & \\ C1 \\ & & \\ F \end{array}$$

RN 314771-69-2 CAPLUS

CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-[(2-methoxy-1-methylethyl)methylamino]- (9CI) (CA INDEX NAME)

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NR?R?

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R?

I
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AB Title compds. [I; Ra = H, alkyl; Rb = (substituted) Ph, PhCH2, PhCH2CH2; Rc = (substituted) cycloalkoxy, cycloalkylalkoxy; A = (alkyl-substituted) imino; B = CO, SO2; C = (substituted) allenylene, vinylene, butadienylene, ethynylene; D = (fluorinated) alkylene, carbonylalkylene, sulfonylalkylene, carbonyloxyalkylene, carbonyliminoalkylene, bond, etc.; E = amino, (substituted) alkylamino, dialkylamino, etc.], were prepd. Thus, 6-amino-4-[(3-bromophenyl)amino]-7-[3-(1-methylpiperidin-4-yl)propoxylquinazoline (prepn. given) in CH2Cl2 contg. Et3N at -10.degree. was treated with acryloyl chloride in THF to give 35% 4-[(3-bromophenyl)amino]-7-[3-(1-methylpiperidin-4-yl)propyloxy]-6-[(vinylcarbonyl)amino]quinazoline. The latter inhibited EGF-dependent proliferation of F/L HERC cells with IC50 = <0.35 nM.

RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

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L4 ANSWER 7 OF 7 CAPLUS COPYRIGHT 2003 ACS
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AN 2000:628125 CAPLUS

DN 133:207919

TI Preparation of 4-amino-quinazoline and quinoline derivatives having an inhibitory effect on signal transduction mediated by tyrosine kinases useful for treating tumoral diseases, lung and respiratory tract diseases

IN Himmelsbach, Frank; Langkopf, Elke; Jung, Birgit; Metz, Thomas; Solca, Flavio; Blech, Stefan

PA Boehringer Ingelheim Pharma K.-G., Germany

SO PCT Int. Appl., 232 pp. CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 2

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PATENT NO.
                      KIND
                            DATE
                                           APPLICATION NO.
                                                             DATE
                      _ _ _ _
PI
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                       A1
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10016280.1 Pa	ge 75		
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PATENT FAMILY INFORMATION:
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US 1999-149329PP 19990817

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OS MARPAT 133:207919

IT290302-11-3P 290302-19-1P 290302-25-9P 290302-39-5P 290302-47-5P 290302-98-6P 290303-04-7P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(prepn. of aminoquinazoline and aminoquinoline derivs. having an inhibitory effect on signal transduction mediated by tyrosine kinases useful for treating tumoral diseases, lung and respiratory tract diseases)

RN 290302-11-3 CAPLUS

CN 1-Piperazineacetic acid, 4-[4-[[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]amino]-4-oxo-2-butenyl]-, ethyl ester (9CI) (CA INDEX NAME)

$$\begin{array}{c} & & & \\ & &$$

RN 290302-19-1 CAPLUS

CN .beta.-Alanine, N-[4-[[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]amino]-4-oxo-2-butenyl]-N-(2-ethoxy-2-oxoethyl)-, ethyl ester (9CI) (CA INDEX NAME)

RN 290302-25-9 CAPLUS

CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-(2-oxo-4-morpholinyl)- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & & & \\ &$$

RN 290302-39-5 CAPLUS

CN 1-Piperazineacetic acid, 4-[4-[[4-[(3-chloro-4-fluorophenyl)amino]-7-(2-

Patel

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cyclopropylethoxy)-6-quinazolinyl]amino]-4-oxo-2-butenyl]-, ethyl ester
(9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & & & \\ &$$

RN 290302-47-5 CAPLUS

CN L-Proline, 1-[4-[[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]amino]-4-oxo-2-butenyl]-, methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry unknown.

RN 290302-98-6 CAPLUS

CN Glycine, N-[2-(acetylthio)ethyl]-N-[4-[[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]amino]-4-oxo-2-butenyl]-, ethyl ester (9CI) (CA INDEX NAME)

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$$\begin{array}{c|c} & & & & \\ & & & \\ & & \\ & & \\ \text{EtO-C-CH}_2 - \text{N-CH}_2 - \text{CH-C-NH} \\ & & \\ & & \\ \text{AcS-CH}_2 - \text{CH}_2 \\ & &$$

RN 290303-04-7 CAPLUS

CN Glycine, N-[2-(acetyloxy)ethyl]-N-[4-[[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]amino]-4-oxo-2-butenyl]-, ethyl ester (9CI) (CA INDEX NAME)

IT 290303-47-8P 290303-74-1P 290303-84-3P 290303-96-7P 290304-01-7P 290304-02-8P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(prepn. of aminoquinazoline and aminoquinoline derivs. having an inhibitory effect on signal transduction mediated by tyrosine kinases useful for treating tumoral diseases, lung and respiratory tract diseases)

RN 290303-47-8 CAPLUS

CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-(1-piperazinyl)- (9CI) (CA INDEX NAME)

RN 290303-74-1 CAPLUS

CN 2-Butenoic acid, 4-[[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]amino]-4-oxo-(9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & & & \\ &$$

RN 290303-84-3 CAPLUS

CN Glycine, N-[4-[[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]amino]-4-oxo-2-butenyl]-N-[2-[(methylsulfonyl)oxy]ethyl]-, ethyl ester (9CI) (CA INDEX NAME)

RN 290303-96-7 CAPLUS

CN 2-Butenoic acid, 4-[[4-[(3-chloro-4-fluorophenyl)amino]-7-

Patel

Page 82

(cyclopropylmethoxy)-6-quinazolinyl]amino]-4-oxo-, ethyl ester (9CI) (CA INDEX NAME)

RN 290304-01-7 CAPLUS

CN 1-Piperazinecarboxylic acid, 4-[4-[[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]amino]-4-oxo-2-butenyl]-,
1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & & & \\ &$$

RN 290304-02-8 CAPLUS

CN 1,3-Piperazinedicarboxylic acid, 4-[4-[[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]amino]-4-oxo-2-butenyl]-, 1-(1,1-dimethylethyl) 3-ethyl ester (9CI) (CA INDEX NAME)

## IT 290303-13-8P

RL: RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)

(prepn. of aminoquinazoline and aminoquinoline derivs. having an inhibitory effect on signal transduction mediated by tyrosine kinases useful for treating tumoral diseases, lung and respiratory tract diseases)

RN 290303-13-8 CAPLUS

CN 2-Piperazinecarboxylic acid, 1-[4-[[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]amino]-4-oxo-2-butenyl]-, ethyl ester (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & & & \\ & & \\ & & \\ N - CH_2 - CH = CH - C - NH \\ & & \\ C - OEt \\ & & \\ O \end{array}$$

1T 290301-79-0P 290301-80-3P 290301-81-4P 290301-82-5P 290301-85-8P 290302-09-9P 290302-15-7P 290302-21-5P 290302-23-7P 290302-27-1P 290302-29-3P 290302-35-1P 290302-37-3P 290302-43-1P 290302-45-3P 290302-49-7P 290302-51-1P 290302-53-3P 290302-55-5P 290302-57-7P 290302-65-7P 290302-61-3P 290302-63-5P 290302-65-7P 290302-81-7P 290302-83-9P 290302-89-5P 290302-91-9P 290302-93-1P 290302-94-2P 290303-00-3P 290303-02-5P 290303-03-65

290303-05-8P 290303-06-9P 290303-07-0P 290303-08-1P 290303-09-2P 290303-10-5P 290303-11-6P 290303-12-7P 290303-14-9P 290303-15-0P 290303-16-1P 290303-17-2P 290303-18-3P

RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(prepn. of aminoquinazoline and aminoquinoline derivs. having an inhibitory effect on signal transduction mediated by tyrosine kinases useful for treating tumoral diseases, lung and respiratory tract diseases)

RN 290301-79-0 CAPLUS

CN Glycine, N-[7-[[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]amino]-4,7-dioxo-5-heptenyl]-N-methyl-, ethyl ester (9CI) (CA INDEX NAME)

EtO-C-CH<sub>2</sub>-N-(CH<sub>2</sub>)<sub>3</sub>-C-CH=CH-C-NH
O Me
O
$$\begin{array}{c|c}
CH_2-O & N \\
NH
O & NH
O & O & O \\
C1 & F
\end{array}$$

RN 290301-80-3 CAPLUS

CN Glycine, N-[6-[[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]amino]-3,6-dioxo-4-hexenyl]-N-methyl-, ethyl ester (9CI) (CA INDEX NAME)

RN 290301-81-4 CAPLUS

CN 1-Piperazineacetic acid, 4-[4-[[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]amino]-1,4-dioxo-2-butenyl]-, ethyl ester (9CI) (CA INDEX NAME)

RN 290301-82-5 CAPLUS
CN L-Proline, 1-[4-[[4-[(3-chloro-4-fluorophenyl)amino]-7(cyclopropylmethoxy)-6-quinazolinyl]amino]-1,4-dioxo-2-butenyl]-, methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry unknown.

RN 290301-85-8 CAPLUS

CN 1-Piperazineacetic acid, 4-[4-[[4-[(3-bromophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]amino]-4-oxo-2-butenyl]-,

[[(1,1-dimethylethoxy)carbonyl]oxy]methyl ester (9CI) (CA INDEX NAME)

RN 290302-09-9 CAPLUS

CN Glycine, N-[4-[[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]amino]-4-oxo-2-butenyl]-N-methyl-, ethyl ester (9CI) (CA INDEX NAME)

RN 290302-15-7 CAPLUS

CN Propanedioic acid, [[4-[[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]amino]-4-oxo-2-butenyl]methylamino]-, dimethyl ester (9CI) (CA INDEX NAME)

RN 290302-21-5 CAPLUS

CN 1-Piperazineacetic acid, 4-[4-[[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]amino]-4-oxo-2-butenyl]-,

1,1-dimethylethyl ester (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & & & \\ &$$

RN 290302-23-7 CAPLUS

CN .beta.-Alanine, N-[4-[[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]amino]-4-oxo-2-butenyl]-N-(3-ethoxy-3-oxopropyl)-, ethyl ester (9CI) (CA INDEX NAME)

RN 290302-27-1 CAPLUS

CN Glycine, N-[4-[[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]amino]-4-oxo-2-butenyl]-N-(2-hydroxyethyl)-, ethyl ester (9CI) (CA INDEX NAME)

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RN 290302-29-3 CAPLUS

CN 1-Piperazineacetic acid, 4-[4-[[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclohexylmethoxy)-6-quinazolinyl]amino]-4-oxo-2-butenyl]-, ethyl ester (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & & & \\ &$$

RN 290302-35-1 CAPLUS

CN 1-Piperazineacetic acid, 4-[4-[[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclobutylmethoxy)-6-quinazolinyl]amino]-4-oxo-2-butenyl]-, ethyl ester (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & & & \\ &$$

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RN 290302-37-3 CAPLUS

CN 1-Piperazineacetic acid, 4-[4-[[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopentylmethoxy)-6-quinazolinyl]amino]-4-oxo-2-butenyl]-, ethyl ester (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & & & \\ &$$

RN 290302-43-1 CAPLUS

CN Glycine, N-[4-[[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]amino]-4-oxo-2-butenyl]-N-(2-hydroxy-2-methylpropyl)-, ethyl ester (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & & \\ & & \\ & & & \\ & &$$

RN 290302-45-3 CAPLUS

CN 2-Piperidinecarboxylic acid, 1-[4-[[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]amino]-4-oxo-2-butenyl]-, methyl ester (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & & & \\ & & \\ & & \\ N - CH_2 - CH = CH - C - NH \\ & & \\ C - OMe \\ & & \\ O \end{array}$$

RN 290302-49-7 CAPLUS

CN Glycine, N-[4-[[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]amino]-4-oxo-2-butenyl]-N-(2-methoxy-2-oxoethyl)-, methyl ester (9CI) (CA INDEX NAME)

RN 290302-51-1 CAPLUS

CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-(5,5-dimethyl-2-oxo-4-morpholinyl)- (9CI) (CA INDEX NAME)

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RN 290302-53-3 CAPLUS

CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-(5-methyl-2-oxo-4-morpholinyl)- (9CI) (CA INDEX NAME)

$$\begin{array}{c} \text{Me} \\ \text{N---} \text{CH}_2\text{---} \text{CH} \\ \text{CH}_2\text{---} \text{CH} \\ \text{O} \\ \text{NH} \\ \text{O} \\ \text{C1} \\ \text{F} \end{array}$$

RN 290302-55-5 CAPLUS

CN D-Proline, 1-[4-[[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]amino]-4-oxo-2-butenyl]-, methyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry unknown.

RN 290302-57-7 CAPLUS

CN 2,5-Pyrrolidinedicarboxylic acid, 1-[4-[[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]amino]-4-oxo-2-butenyl]-, diethyl ester, (2R,5S)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.

Double bond geometry unknown.

RN 290302-59-9 CAPLUS

CN 2,6-Piperidinedicarboxylic acid, 1-[4-[[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]amino]-4-oxo-2-butenyl]-, dimethyl ester, (2R,6S)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry. Double bond geometry unknown.

RN 290302-61-3 CAPLUS

CN 2,6-Piperidinedicarboxylic acid, 1-[4-[[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]amino]-4-oxo-2-butenyl]-, dimethyl ester, (2R,6R)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.

Double bond geometry unknown.

RN 290302-63-5 CAPLUS

CN 2,5-Pyrrolidinedicarboxylic acid, 1-[4-[[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]amino]-4-oxo-2-butenyl]-, dimethyl ester, (2R,5S)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.

Double bond geometry unknown.

RN 290302-65-7 CAPLUS

CN 2,5-Pyrrolidinedicarboxylic acid, 1-[4-[[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]amino]-4-oxo-2-butenyl]-, dimethyl ester, (2R,5R)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.
Double bond geometry unknown.

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RN 290302-67-9 CAPLUS

CN 1-Piperazineacetic acid, 4-[4-[[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]amino]-1-methyl-4-oxo-2-butenyl]-, ethyl ester (9CI) (CA INDEX NAME)

RN 290302-71-5 CAPLUS

CN Alanine, N-[4-[[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]amino]-4-oxo-2-butenyl]-N-methyl-, methyl ester (9CI) (CA INDEX NAME)

RN 290302-73-7 CAPLUS

CN L-Proline, 1-[4-[[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]amino]-4-oxo-2-butenyl]-, phenylmethylester (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.

RN 290302-81-7 CAPLUS

CN 2-Piperidineacetic acid, 1-[4-[[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]amino]-4-oxo-2-butenyl]-, ethyl ester (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & & & \\ & & \\ & & \\ N - CH_2 - CH = CH - C - NH \\ & & \\ CH_2 - C - OEt \\ & & \\ C1 \\ & &$$

RN 290302-83-9 CAPLUS

CN Alanine, N-[4-[[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]amino]-4-oxo-2-butenyl]-N-(2-ethoxy-2-oxoethyl)-, ethyl ester (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & & & & & & \\ & & & & & \\ & & & & \\ & & & & \\ EtO-C-CH-N-CH_2-CH-CH-C-NH \\ & & & & \\ EtO-C-CH_2 \\ & & & \\ & &$$

RN 290302-89-5 CAPLUS

CN D-Alanine, N-[4-[[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]amino]-4-oxo-2-butenyl]-N-(2-hydroxyethyl)-, ethyl ester (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry unknown.

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RN 290302-91-9 CAPLUS

CN 1H-1,4-Diazepine-1-acetic acid, 4-[4-[[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]amino]-4-oxo-2-butenyl]hexahydro-, ethyl ester (9CI) (CA INDEX NAME)

RN 290302-93-1 CAPLUS

CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-[methyl(tetrahydro-2-oxo-3-furanyl)amino]- (9CI) (CA INDEX NAME)

$$\begin{array}{c} & & & & \\ & & & \\$$

RN 290302-94-2 CAPLUS

CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-[methyl(tetrahydro-5-oxo-3-furanyl)amino]- (9CI) (CA INDEX NAME)

RN 290303-00-3 CAPLUS

CN 1-Piperazineacetic acid, 4-[4-[[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]amino]-4-oxo-2-butenyl]- (9CI) (CA INDEX NAME)

$$\begin{array}{c} & & & \\ & &$$

RN 290303-02-5 CAPLUS

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CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-(2,2-dimethyl-6-oxo-4-morpholinyl)- (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} \text{Me} & \text{Me} \\ \hline \\ \text{O} & \text{N---} \text{CH}_2\text{---} \text{CH---} \text{C---} \text{NH} \\ \hline \\ \text{O} & \text{NH} \\ \hline \\ \text{C1} & \text{F} \\ \end{array}$$

RN 290303-03-6 CAPLUS

CN 2-Butenamide, N-[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]-4-[(3R)-3-methyl-2-oxo-4-morpholinyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry unknown.

RN 290303-05-8 CAPLUS

CN 1-Piperazineacetic acid, 4-[4-[[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]amino]-4-oxo-2-butenyl]-, phenylmethyl ester (9CI) (CA INDEX NAME)

RN 290303-06-9 CAPLUS

CN 1-Piperazineacetic acid, 4-[4-[[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]amino]-4-oxo-2-butenyl]-, phenyl ester (9CI) (CA INDEX NAME)

$$\begin{array}{c|c} & & & \\ &$$

RN 290303-07-0 CAPLUS

CN 1-Piperazineacetic acid, 4-[4-[[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]amino]-4-oxo-2-butenyl]-, 2,3-dihydro-1H-inden-5-yl ester (9CI) (CA INDEX NAME)

RN 290303-08-1 CAPLUS

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CN 1-Piperazineacetic acid, 4-[4-[[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]amino]-4-oxo-2-butenyl]-, cyclohexylmethyl ester (9CI) (CA INDEX NAME)

RN 290303-09-2 CAPLUS

CN 1-Piperazineacetic acid, 4-[4-[[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]amino]-4-oxo-2-butenyl]-, octyl ester (9CI) (CA INDEX NAME)

Me- (CH<sub>2</sub>)<sub>7</sub>-O-C-CH<sub>2</sub>

$$0$$

$$N$$

$$N$$

$$CH_2$$

$$CH_2$$

$$O$$

$$NH$$

$$O$$

$$CH_2$$

$$O$$

$$O$$

$$NH$$

$$O$$

RN 290303-10-5 CAPLUS

CN 1-Piperazineacetic acid, 4-[4-[[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]amino]-4-oxo-2-butenyl]-, hexyl ester (9CI) (CA INDEX NAME)

Me- (CH<sub>2</sub>)<sub>5</sub>-O-C-CH<sub>2</sub>

$$0$$

$$N$$

$$N$$

$$CH_2$$

$$CH_2$$

$$CH_2$$

$$O$$

$$NH$$

$$O$$

$$C1$$

$$E$$

RN 290303-11-6 CAPLUS

CN 1-Piperazineacetic acid, 4-[4-[[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]amino]-4-oxo-2-butenyl]-3-(ethoxycarbonyl)-, ethyl ester (9CI) (CA INDEX NAME)

RN 290303-12-7 CAPLUS

CN 1-Piperazinebutanoic acid, 4-[4-[[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]amino]-4-oxo-2-butenyl]-, ethyl ester (9CI) (CA INDEX NAME)

RN 290303-14-9 CAPLUS

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CN 2-Piperazinecarboxylic acid, 1-[4-[[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]amino]-4-oxo-2-butenyl]-4-methyl-, ethyl ester (9CI) (CA INDEX NAME)

RN 290303-15-0 CAPLUS

CN 2-Piperazinecarboxylic acid, 1-[4-[[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]amino]-4-oxo-2-butenyl]-4-(methylsulfonyl)-, ethyl ester (9CI) (CA INDEX NAME)

RN 290303-16-1 CAPLUS

CN 1-Piperazinepropanoic acid, 4-[4-[[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]amino]-4-oxo-2-butenyl]-, ethyl ester (9CI) (CA INDEX NAME)

$$\begin{array}{c} & & & & \\ & & & \\$$

RN 290303-17-2 CAPLUS

CN 1-Piperazineacetic acid, 4-[4-[[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]amino]-1,1-dimethyl-4-oxo-2-butenyl]-, ethyl ester (9CI) (CA INDEX NAME)

RN 290303-18-3 CAPLUS

CN 2-Piperazinecarboxylic acid, 4-acetyl-1-[4-[[4-[(3-chloro-4-fluorophenyl)amino]-7-(cyclopropylmethoxy)-6-quinazolinyl]amino]-4-oxo-2-butenyl]-, ethyl ester (9CI) (CA INDEX NAME)

GI

Title compds. [I; R1 = H, C1-C4-alkyl; R2 = (un)substituted Ph, benzyl, 1-phenylethyl; R3, R4 independently = H, F, C1, CH3O, CH3OCH2, (CH3)2NCH2, (CH3CH2)2NCH2, pyrrolidino, piperidino, morpholino; X = C(CN), N; A = O, NH, (C1-C4)-alkylN; B = CO, SO2; C = 1,3-allenylene, 1,1-vinylene, 1,2-vinylene, 1,3-butadien-1,4-ylene, with CH3, CF3 substitution; D = alkylene, CO-alkylene, SO2-alkylene; CO, SO2; E = HOCO(CH2)nNR5, (HO)2P(:O)(CH2)nNR5; n = 1-6; R5 = H, alkyl], tautomers, stereoisomers, and physiol. acceptable salts are prepd. and having valuable pharmacol. properties, particularly an inhibiting effect on signal transduction mediated by tyrosine kinases. Title compds. are useful for treating tumoral diseases, diseases of the lungs and respiratory tract. Thus, the title compd. II was prepd. and tested by Cell Titer 96TM Aq. Nonradioactive Cell Proliferation Assay.

RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD ALL CITATIONS AVAILABLE IN THE RE FORMAT

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SEARCH CHARGES	0.00	147.75
DISPLAY CHARGES	47.49	47.49
	47.89	196.25
CAPLUS FEE (5%)	2.39	_ 2.39
FULL ESTIMATED COST		
FULL ESTIMATED COST	50.28	198.64

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